would our message need to change once more? Here are the facts: hepatitis C virus is common among Americans born between 1945 and 1965. A current Centers for Disease Control and Prevention factsheet asserts that most people infected with hepatitis C virus are unaware of their diagnosis,[3] despite aggressive campaigns since 2012 to find cases. Let's just go ahead and test our baby boomers.

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ACS has received grants and personal fees from Gilead Sciences and grants from Bristol-Myers Squibb. LSM has received funding from Bristol-Myers Squibb and grants from Gilead Sciences. They both have received grants from and worked on various projects with members of the Centers for Disease Control and Prevention Division of Viral Hepatitis.

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Long-term surveillance of the effect of PCV13: the future challenge in Africa

Pneumococcal infections are a leading cause of morbidity and mortality in children. In Africa, the greatest burden of pneumococcal disease and most associated deaths occur in children younger than 5 years.[1] In 2008, this continent still accounted for more than half of the 541 000 deaths caused by pneumococcal disease in this age group.[2]

The effectiveness of the seven-valent pneumococcal conjugate vaccine (PCV7) has been shown in many countries—the incidence of invasive pneumococcal disease has fallen in all age groups, especially in children younger than 2 years.[3] However, in some countries, this decrease was mitigated by an increased incidence of invasive pneumococcal disease caused by non-vaccine serotypes, most belonging to the extended-spectrum PCV.[4] Soon after the switch from PCV7 to PCV13, many countries such as the USA, France, the UK, and Israel reported the expected pronounced decrease in invasive pneumococcal disease.[5–8] The high effectiveness of the PCV10 vaccine has also been shown in Finland for invasive pneumococcal disease and clinically suspected invasive pneumococcal disease.[9]

These results led to PCVs being classified among the more potent available vaccines: in the USA, 55 000 deaths from pneumococcus-related diseases in children were prevented by PCVs between 2001 and 2013.[10] However, in developed countries, which benefit from favourable living conditions and well organised health-care systems, the early (and sustained) assessment of PCV performance is helped by active and well established surveillance of invasive pneumococcal disease. The burden of invasive pneumococcal disease remains highest in low-income countries. Some had introduced PCVs through the GAVI Alliance with a small self-financed contribution. However, little published evidence is available about the effect of PCVs on invasive pneumococcal disease in this context, because of the challenges in surveillance.

In *The Lancet Infectious Diseases*, Grant Mackenzie and colleagues report the results of a well designed population-based active and standardised surveillance study for invasive pneumococcal disease in


Shehzad Noorani/AP/Press Association Images

Published Online
February 17, 2016
http://dx.doi.org/10.1016/S1473-3099(16)00059-1

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The Gambia before and after PCV implementation (PCV7 in 2009 and PCV13 in 2011).[11] Apart from the reported expected findings, of significance is the admirable effort by the authors to do such a study by rigorously standardising the clinical and laboratory aspects of the surveillance. The project involved several teams, with conceptualisation beginning about 10 years ago. The authors investigated 14 650 patients and identified 320 cases of invasive pneumococcal disease, to do a robust assessment of the effect of PCV13. Despite suboptimal PCV13 coverage, in children 2–23 months of age, the incidence of invasive pneumococcal disease fell by 55% (95% CI 30–71) and that of PCV13 serotype prevalence fell by 82% (95% CI 64–91). In older children (2–4 years of age), the incidence of invasive pneumococcal disease fell by 56% (95% CI 25–75) owing to a 68% (95% CI 39–83) reduction in the prevalence of PCV13 serotypes, which suggests that a combination of direct and herd protection effects were in force.

All these results support the substantial benefit of PCVs introduced in African countries. However, two concerns draw our attention: first, the report of a slight increase in invasive pneumococcal disease incidence in all age groups (except adults) in 2014, and second, a significant increase in prevalence of non-PCV13 serotypes, especially in children aged 2–59 months, in whom the incidence of invasive pneumococcal disease almost doubled. This potentially worrying result should be balanced by the fact that the serotypes that emerged are unlikely to be as invasive as those included in the PCVs.[12] In the post-PCV13 era, the main non-PCV13 serotypes that the authors reported in children 2–59 months old were serotypes 12F, 10A, 15A, 35B, and 16F.[11] A recent study showed that of the non-PCV13 serotypes, only two—24F and 12F—had high disease potential in the PCV13 era.[12] In Mackenzie and colleagues' study in The Gambia, serotype 24F was rare (only two cases were reported) in the PCV13 era, so serotype 12F remained the only one with high disease-causing potential.[11]

Besides the reduced incidence of invasive pneumococcal disease in developed countries, the spectrum and profile of invasive pneumococcal disease has changed following the changed serotype distribution, and the proportion of patients with underlying illnesses has increased.[13] We have shown that patients with meningitis are infected more frequently with non-PCV13 serotypes than other serotypes, whereas serotypes implicated in pneumococcal pneumonia are usually PCV13 serotypes, especially 1, 7F, 19A, and 3.[13] These results agree with those reported by Kaplan and colleagues,[14] showing greater reduction in cases of pneumococcal bacteraemia, pneumonia, and mastoiditis than those of meningitis after PCV13 introduction in eight children's hospitals in the USA. Similarly, the data reported by Mackenzie and colleagues[11] show that patients with meningitis were infected more frequently with non-PCV13 serotypes than PCV13 serotypes (44·7% *vs* 26·3%), whereas for pneumonia, the rates were reversed (21·7% *vs* 56·1%).[11] This serotype distribution clearly explains the notable decrease in pneumonia cases and the slight fall in meningitis cases. With a more prolonged period after PCV13 introduction, the expected decrease in pneumonia cases will be substantial.

This study has important implications for the introduction of PCVs in all African countries, where the rates of invasive pneumococcal disease remain around ten-fold higher than those in developed countries. However, maintenance of invasive pneumococcal disease surveillance is essential to clarify the role of PCVs in changing the serotype incidence, in view of the possible increase in invasive pneumococcal disease cases related to non-vaccine serotypes.

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The authors' institution (ACTIV) has received research grant support from Pfizer, GlaxoSmithKline, and Sanofi Pasteur MSD. CL has received personal fees from Pfizer and Novartis outside the submitted work. RC has received personal fees from Pfizer, GSK, Sanofi, and Novartis outside the submitted work.

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The elusive global burden of dengue

Published **Online** February 10, 2016 http://dx.doi.org/10.1016/S1473-3099(16)00076-1

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Dengue has emerged in the past two decades as a rapidly growing and widespread public health problem, with over half of the world's countries and people now at risk.[1] In new estimates from the Global Burden of Disease study published in *The Lancet Infectious Diseases*, Jeffrey Stanaway and colleagues[2] suggest that dengue incidence has increased six-fold from 1990 to 2013, accompanied by much flatter mortality trends. Dengue is still regarded as a neglected disease,[3] yet its incidence is increasing at an alarming rate, by contrast with declines in other neglected diseases.[4] WHO estimates that 50 million to 100 million cases occur annually.[5] In 2012, however, formal modelling put the number of dengue infections as high as 390 million (95% credible interval 284 million–528 million), but included both inapparent and apparent cases.[1] Their estimated number of apparent cases (96 million, 95% credible interval 67 million–136 million) lies at the high end of the WHO estimates.

Against this background, these new estimates from the Global Burden of Disease Study suggest a much lower number of cases for 2013: 58·4 million (95% uncertainty interval 23·6 million–121·9 million).[2] Why is it so difficult to arrive at consistent estimates?

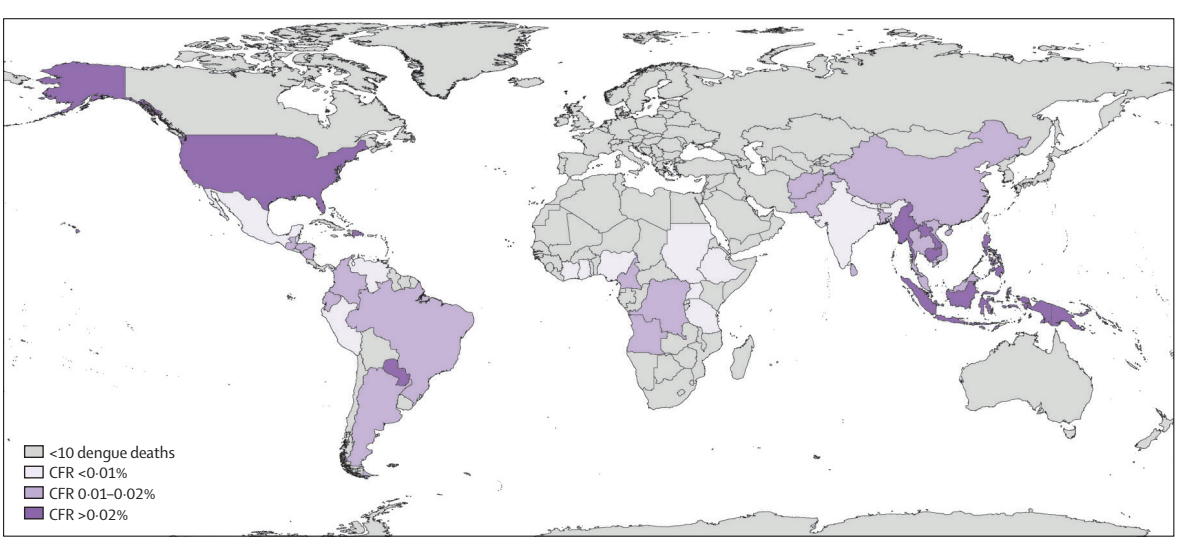

Figure: **Dengue case fatality rates for 39 countries estimated to have at least ten dengue deaths and autochthonous transmission**
Data from Stanaway and colleagues.[2] CFR=case fatality rate.